L Number	Hits	Search Text	DB	Time stamp
1	11024	granulocyte	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/03/12 12:30
2	183	granulocyte SAME "gene expression"	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/03/12 12:30
3	24	(granulocyte SAME "gene expression") SAME differential	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/03/12 12:33
4	2	6365352.pn.	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/03/12 12:52
5	15595	neutrophils or eosinophils or basophils	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/03/12 12:52
7	0	(neutrophils or eosinophils or basophils) SAME "gene expression differential"	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/03/12 12:53
8	19	(neutrophils or eosinophils or basophils) and "gene expression differential"	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/03/12 12:57
9	8687	"inflammatory disease"	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/03/12 12:57
10	122097	glomerulonephritis or psoriasis or rheumatoid arthritis or asthma or thrombosis or "periodontal disease" or "inflammatory bowel disease"	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/03/12 12:59
11	16535	"crohn's disease" or colitis	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/03/12 12:59
6	59	"gene expression differential"	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/03/12 13:01
14	2	"gene expression differential" and "inflammatory disease"	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/03/12 13:01
13	20	"gene expression differential" and (glomerulonephritis or psoriasis or rheumatoid arthritis or asthma or thrombosis or "periodontal disease" or "inflammatory bowel disease")	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/03/12 13:05
12	12	"gene expression differential" and ("crohn's disease" or colitis)	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/03/12 13:01
16	3432	(neutrophils or eosinophils or basophils) SAME (glomerulonephritis or psoriasis or rheumatoid arthritis or asthma or thrombosis or "periodontal disease" or "inflammatory bowel disease")	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/03/12 13:05
17	583	(neutrophils or eosinophils or basophils) SAME ("crohn's disease" or colitis)	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/03/12 13:05
18	4	((neutrophils or eosinophils or basophils) SAME "inflammatory disease") SAME "expression profile"	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/03/12 13:06

20	3032	"expression profile"	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/03/12 13:06
21	0	((neutrophils or eosinophils or basophils) SAME (glomerulonephritis or psoriasis or rheumatoid arthritis or asthma or thrombosis or "periodontal disease" or "inflammatory bowel disease")) SAME "1120"	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/03/12 13:06
25	11	((neutrophils or eosinophils or basophils) SAME (glomerulonephritis or psoriasis or rheumatoid arthritis or asthma or thrombosis or "periodontal disease" or "inflammatory bowel disease")) and "129"	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/03/12 13:07
23	5	((neutrophils or eosinophils or basophils) SAME ("crohn's disease" or colitis)) SAME "expression profile"	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/03/12 13:07
22	16	((neutrophils or eosinophils or basophils) SAME (glomerulonephritis or psoriasis or rheumatoid arthritis or asthma or thrombosis or "periodontal disease" or "inflammatory bowel disease")) SAME "expression profile"	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/03/12 13:07
19	12	((neutrophils or eosinophils or basophils) SAME "inflammatory disease") and "expression profile"	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/03/12 13:07
24	150	((neutrophils or eosinophils or basophils) SAME ("crohn's disease" or colitis)) and "expression profile"	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/03/12 13:09
26	183	((neutrophils or eosinophils or basophils) SAME (glomerulonephritis or psoriasis or rheumatoid arthritis or asthma or thrombosis or "periodontal disease" or "inflammatory bowel disease")) and "expression profile"	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/03/12 13:16
15	267	(neutrophils or eosinophils or basophils) SAME "inflammatory disease"	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/03/12 13:12
28	7	"sterile inflammatory disease"	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/03/12 13:16

FILE 'MEDLINE, EMBASE, BIOSIS' ENTERED AT 13:51:52 ON 12 MAR 2004

L1	364	S GRANULOCYTE AND "INFLAMMATORY DISEASE"
L2	253	DUP REM L1 (111 DUPLICATES REMOVED)
L3	20	S L2 AND "GENE EXPRESSION"
L4	20	S L3 NOT PY
L5	10	S L3 NOT PY>=1998
L6	27822	S "INFLAMMATORY DISEASE"
L7	620	S L6 AND "GENE EXPRESSION"
L8	473	DUP REM L7 (147 DUPLICATES REMOVED)
L9	159	S L8 NOT PY>=1998
L10	10	S L9 AND GRANULOCYTE
L11	23308	S MICROARRAY
L12	31	S L11 AND L6
L13	22	DUP REM L12 (9 DUPLICATES REMOVED)
L14	1	S L13 NOT PY>=1998

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 FILE 'MEDLINE, EMBASE, BIOSIS' ENTERED AT 13:28:18 ON 12 MAR 2004
L1       294259 S GRANULOCYTE OR NEUTROPHIL OR EOSINOPHIL OR BASOPHIL
L2         2875 S "GENE EXPRESSION DIFFERENTIAL" OR "GENE EXPRESSION PROFILE"
L3            9 S "STERILE INFLAMMATORY DISEASE"
L4        27822 S "INFLAMMATORY DISEASE"
L5        85263 S "GLOMERULONEPHRITIS OR PSORIASIS OR "RHEUMATOID ARTHRITIS" OR
L6            0 S L1 AND L2 AND L3 AND L4 AND L5
L7           61 S L1 AND L2
L8           36 S L1 (P) L2
L9            1 S L1 AND L3
L10        1311 S L1 AND L4
L11         611 S L1 (P) L4
L12          58 S L10 AND L5
L13          21 S L11 AND L5
L14          39 DUP REM L7 (22 DUPLICATES REMOVED)
L15          16 DUP REM L8 (20 DUPLICATES REMOVED)
L16          43 DUP REM L12 (15 DUPLICATES REMOVED)
L17          11 DUP REM L13 (10 DUPLICATES REMOVED)
L18           5 S L14 NOT PY>=1998
L19           3 S L15 NOT PY>=1998
L20          19 S L16 NOT PY>=1998
L21           4 S L17 NOT PY>=1998
L22           4 DUP REM L3 (5 DUPLICATES REMOVED)
L23           1 S L22 NOT PY>=1998
L24           5 S L2 AND L4
L25           3 DUP REM L24 (2 DUPLICATES REMOVED)
L26           0 S L25 NOT PY>=1998
L27           7 S L2 AND L5
L28           2 DUP REM L27 (5 DUPLICATES REMOVED)
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FILE 'MEDLINE, EMBASE, BIOSIS' ENTERED AT 14:07:40 ON 12 MAR 2004
L1         26838 S "DIFFERENTIAL EXPRESSION"
L2         56993 S DIFFERENTIAL (S) EXPRESSION
L3        294259 S GRANULOCYTE OR NEUTROPHIL OR BASOPHIL OR EOSINOPHIL
L4          1112 S L2 AND L3
L5           543 S L4 NOT PY>=1998
L6           317 DUP REM L5 (226 DUPLICATES REMOVED)
L7             0 S L6 AND (MICROARRAY OR "HIGH THROUGH" OR "EXPRESSION PROFILE"
L8             0 S L6 AND MICROARRAY
L9             2 S L6 AND AUTOIMMUNE
L10            8 S L6 AND MODULATE
```

Ehlers S; Mielke M E; Hahn H
CORPORATE SOURCE: Institut fur Medizinische Mikrobiologie und Infektionsimmunologie, Freie Universitat Berlin, Germany.
SOURCE: International immunology, (1994 Nov) 6 (11) 1727-37.
Journal code: 8916182. ISSN: 0953-8178.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; AIDS
ENTRY MONTH: 199503
ENTRY DATE: Entered STN: 19950407
Last Updated on STN: 19950407
Entered Medline: 19950330

AB In murine listeriosis, elimination of bacteria and immunity to re-infection critically depend on Thy-1+CD4- cells, while cell-mediated inflammatory phenomena like delayed-type hypersensitivity and granuloma formation are mediated by CD4+ T cells. In an attempt to correlate T cell phenotype and function with a particular set of cytokines produced in vivo, we examined the cytokine **gene expression profile** associated with the presence or absence of CD4+ and/or CD8+ cells in the livers of mice during experimental infection with Listeria monocytogenes. T cell subset depletion was achieved by i.p. administration of saturating amounts of the appropriate mAbs, and mRNA detection was carried out using a qualitative and semi-quantitative polymerase chain reaction-based mRNA amplification protocol. In both primary and secondary infection, the presence of CD4+ cells was a prerequisite for granuloma formation, and was found to be closely associated with mRNA expression for IL-2, IL-3 and IL-4, a 5-fold increase in expression of tumor necrosis factor (TNF)-alpha and **granulocyte** macrophage colony stimulating factor, and a 25-fold increase in expression of IFN-gamma and TNF-beta mRNAs, suggesting a role for these cytokines in granuloma formation. In striking contrast, depletion of CD8+ cells did not result in reduced mRNA expression for any one of the cytokines studied, implying that CD8+ T cell mediated cure and prevention of listeriosis may operate via qualitatively distinct mechanisms.

NSWER 19 OF 19 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 1991:27199 BIOSIS
DOCUMENT NUMBER: PREV199191016550; BA91:16550
TITLE: METABOLIC AND PHAGOCYTIC ACTIVITY OF **NEUTROPHIL** GRANULOCYTES IN PATIENTS WITH UNSPECIFIC ULCERATIVE **COLITIS** AND CROHN'S DISEASE OF THE COLON.
AUTHOR(S): BLAZHENKO I L [Reprint author]; BYCHKOVA N G; ZHVETS N I
CORPORATE SOURCE: DIV FAC THER 1, KIEV MED INST, KIEV, USSR
SOURCE: Vrachebnoe Delo, (1990) No. 6, pp. 61-63.
CODEN: VRDEA5. ISSN: 0049-6804.
DOCUMENT TYPE: Article
FILE SEGMENT: BA
LANGUAGE: RUSSIAN
ENTRY DATE: Entered STN: 3 Jan 1991
Last Updated on STN: 3 Jan 1991

AB Immune homeostasis is of importance in the pathogenesis of unspecific inflammatory diseases of the colon. The authors studied the state of unspecific resistance of patients with unspecific ulcerative **colitis** (UUC) and Crohn's disease (KD); 27 with UUC and 21 KD patients with chronic relapsing forms of the disease were examined. Patients in the acute form of the disease showed an activation of the metabolic processes in the **neutrophil** granulocytes that was more pronounced in UUC and a reduction of the phagocytic activity in KD. During the period of early remission these values were practically normal evidencing the prognostic value of factors of unspecific defense in unspecific inflammatory diseases of the intestine.

N NUMBER: 2001287011 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11278252
TITLE: **Gene expression profile** of antithrombotic protein c defines new mechanisms modulating inflammation and apoptosis.
AUTHOR: Joyce D E; Gelbert L; Ciaccia A; DeHoff B; Grinnell B W
CORPORATE SOURCE: Division of Research Technologies, Lilly Research Laboratories, Lilly Corporate Center, Indianapolis, Indiana 46285, USA.
SOURCE: Journal of biological chemistry, (2001 Apr 6) 276 (14) 11199-203.
Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200105
ENTRY DATE: Entered STN: 20010529
Last Updated on STN: 20030105
Entered Medline: 20010524

AB Human protein C is a natural anticoagulant factor, and a recombinant activated form of the molecule (rhAPC) is completing clinical evaluation for treatment of severe sepsis. Because of the pathophysiologic role of endothelial dysfunction in severe **inflammatory disease** and sepsis, we explored the possibility that rhAPC might directly modulate endothelial function, independent of its anticoagulant activity. Using broad transcriptional profiling, we show that rhAPC directly modulates patterns of endothelial cell gene expression clustering into anti-inflammatory and cell survival pathways. rhAPC directly suppressed expression of p50 and p52 NFkappaB subunits, resulting in a functional decrease in NFkappaB binding at target sites. Further, rhAPC blocked expression of downstream NFkappaB regulated genes following tumor necrosis factor alpha induction, including dose-dependent suppression of cell adhesion expression and functional binding of intracellular adhesion molecule 1, vascular cell adhesion molecule 1, and E-selectin. Further, rhAPC modulated several genes in the endothelial apoptosis pathway, including the Bcl-2 homologue protein and inhibitor of apoptosis protein. These pathway changes resulted in the ability of rhAPC to inhibit the induction of apoptosis by the potent inducer, staurosporine. This new mechanistic understanding of endothelial regulation and the modulation of tumor necrosis factor-induced endothelial dysfunction creates a novel link between coagulation, inflammation, and cell death and provides insight into the molecular basis for the efficacy of APC in systemic inflammation and sepsis.

=>

ANSWER 10 OF 159 MEDLINE on STN
ACCESSION NUMBER: 97225921 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9122163
TITLE: Discovery and analysis of **inflammatory disease**-related genes using cDNA microarrays.
AUTHOR: Heller R A; Schena M; Chai A; Shalon D; Bedilion T; Gilmore J; Woolley D E; Davis R W
CORPORATE SOURCE: Department of Biochemistry, Beckman Center, Stanford University Medical Center, CA 94305, USA.
CONTRACT NUMBER: HG00205 (NHGRI)
R37HG00198 (NHGRI)
SOURCE: Proceedings of the National Academy of Sciences of the United States of America, (1997 Mar 18) 94 (6) 2150-5.
Journal code: 7505876. ISSN: 0027-8424.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199704
ENTRY DATE: Entered STN: 19970506
Last Updated on STN: 20000303
Entered Medline: 19970424

AB cDNA microarray technology is used to profile complex diseases and discover novel disease-related genes. In **inflammatory disease** such as rheumatoid arthritis, expression patterns of diverse cell types contribute to the pathology. We have monitored **gene expression** in this disease state with a microarray of selected human genes of probable significance in inflammation as well as with genes expressed in peripheral human blood cells. Messenger RNA from cultured macrophages, chondrocyte cell lines, primary chondrocytes, and synoviocytes provided expression profiles for the selected cytokines, chemokines, DNA binding proteins, and matrix-degrading metalloproteinases. Comparisons between tissue samples of rheumatoid arthritis and inflammatory bowel disease verified the involvement of many genes and revealed novel participation of the cytokine interleukin 3, chemokine Gro alpha and the metalloproteinase matrix metallo-elastase in both diseases. From the peripheral blood library, tissue inhibitor of metalloproteinase 1, ferritin light chain, and manganese superoxide dismutase genes were identified as expressed differentially in rheumatoid arthritis compared with inflammatory bowel disease. These results successfully demonstrate the use of the cDNA microarray system as a general approach for dissecting human diseases.

=>

TITLE: Chemokines are expressed in a myeloid cell-dependent fashion and mediate distinct functions in immune complex glomerulonephritis in rat.

AUTHOR: Wu X; Dolecki G J; Sherry B; Zagorski J; Lefkowith J B
CORPORATE SOURCE: Department of Medicine, Washington University School of Medicine, St. Louis, MO 63110, USA.

CONTRACT NUMBER: AR-07279 (NIAMS)
SOURCE: Journal of immunology (Baltimore, Md. : 1950), (1997 Apr 15) 158 (8) 3917-24.
Journal code: 2985117R. ISSN: 0022-1767.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199705
ENTRY DATE: Entered STN: 19970514
Last Updated on STN: 19970514
Entered Medline: 19970505

AB Using anti-glomerular basement membrane nephritis in rats, we investigated the mechanisms underlying in situ chemokine expression and the in vivo function of these cytokines during the acute phase of this model. We observed that CXC chemokine expression was monophasic and paralleled **neutrophil** (PMN) influx, whereas CC chemokine expression was biphasic with peaks coinciding with the influx of PMNs and macrophages (Mphi). The initial peak of chemokine expression was attenuated by decomplementation, neutropenia, and leukopenia, while the latter peak was attenuated only by leukopenia and augmented in the accelerated form of this disease model, corresponding to an increase in Mphi influx. **Differential expression** of chemokines by PMNs and Mphi was not an intrinsic property of these cells, as these leukocytes expressed similar profiles of chemokines in vitro. Immunostaining for Mphi inflammatory protein-1alpha, a CC chemokine, in acute nephritis validated that expression during acute nephritis was accompanied by local protein production. Moreover, neutralizing Ab to Mphi inflammatory protein-1alpha attenuated the acute phase proteinuria, but not the accompanying influx of PMNs. Neutralizing Ab to cytokine-induced

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on STN

ACCESSION NUMBER: 96133522 EMBASE
DOCUMENT NUMBER: 1996133522
TITLE: Role of cytokines in rheumatoid arthritis.
AUTHOR: Feldmann M.; Brennan F.M.; Maini R.N.
CORPORATE SOURCE: MTKIR, Hammersmith,W6 8LW London, United Kingdom
SOURCE: Annual Review of Immunology, (1996) 14/- (397-440).
ISSN: 0732-0582 CODEN: ARIMDU
COUNTRY: United States
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 026 Immunology, Serology and Transplantation
031 Arthritis and Rheumatism
LANGUAGE: English
SUMMARY LANGUAGE: English

AB Analysis of cytokine mRNA and protein in rheumatoid arthritis tissue revealed that many proinflammatory cytokines such as TNFα, IL-1, IL-6, GM- CSF, and chemokines such as IL-8 are abundant in all patients regardless of therapy. This is compensated to some degree by the increased production of anti-inflammatory cytokines such as IL-10 and TGFβ and cytokine inhibitors such as IL-1ra and soluble TNF-R. However, this upregulation in homeostatic regulatory mechanisms is not sufficient as these are unable to neutralize all the TNFα and IL-1 produced. In rheumatoid joint cell cultures that spontaneously produce IL-1, TNFα was the major dominant regulator of IL-1. Subsequently, other proinflammatory cytokines were also inhibited if TNFα was neutralized, leading to the new concept that the proinflammatory cytokines were linked in a network with TNFα at its apex. This led to the hypothesis that TNFα was of major importance in rheumatoid arthritis and was a therapeutic target. This hypothesis has been successfully tested in animal models, of, for example, collagen-induced arthritis, and these studies have provided the rationale for clinical trials of anti-TNFα therapy in patients with long-standing rheumatoid arthritis. Several

TLE: Differential regulation of proinflammatory and hematopoietic cytokines in human macrophages after infection with human immunodeficiency virus.

AUTHOR: Esser R; Glienke W; von Briesen H; Rubsamen-Waigmann H; Andreesen R

CORPORATE SOURCE: Georg-Speyer-Haus, Frankfurt am Main, Germany.

SOURCE: Blood, (1996 Nov 1) 88 (9) 3474-81.
Journal code: 7603509. ISSN: 0006-4971.

PUB. COUNTRY: United States

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals; AIDS

ENTRY MONTH: 199612

ENTRY DATE: Entered STN: 19970128
Last Updated on STN: 19970128
Entered Medline: 19961216

AB Cells of the macrophage lineage (MAC) play an important role in human immunodeficiency virus (HIV) infection. However, the knowledge on the extent of macrophage involvement in the pathogenesis of HIV infection is still incomplete. In this study we examined the secretory repertoire of HIV-infected MAC with respect to the proinflammatory cytokines tumor necrosis factor-alpha (TNF-alpha), interleukin-1 beta (IL-1 beta), IL-6, IL-8, and the hematopoietic growth factors M-, G- and **granulocyte** -macrophage colony stimulating factor (GM-CSF). Using a culture system on hydrophobic teflon membranes, blood-derived MO from healthy donors were infected with a monocytotropic HIV-1 isolate (HIV-1D117IIII). We analyzed the constitutive and lipopolysaccharides-stimulated secretion of MO/MAC early after infection as well as in long-term cultured, virus-replicating cells. The release of proinflammatory mediators and hematopoietic growth factors were differentially regulated after infection with HIV: the secretion of TNF-alpha, IL-1 beta, IL-6, IL-8 was upregulated, whereas a down-regulation of M-, G-, and GM-CSF could be observed. These results may provide some explanation for the immunological dysfunction, the hematopoietic failure and the chronic **inflammatory disease** occurring in HIV-infected patients.

ANSWER 3 OF 10 MEDLINE on STN
ACCESSION NUMBER: 96098584 MEDLINE
DOCUMENT NUMBER: PubMed ID: 7500241
TITLE: Interleukin-1 beta **gene expression** in human oral polymorphonuclear leukocytes.
AUTHOR: Hendley T M; Steed R B; Galbraith G M
CORPORATE SOURCE: College of Dental Medicine, Medical University of South Carolina, Charleston, USA.
CONTRACT NUMBER: DE10536 (NIDCR)
SOURCE: Journal of periodontology, (1995 Sep) 66 (9) 761-5.
Journal code: 8000345. ISSN: 0022-3492.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Dental Journals; Priority Journals
ENTRY MONTH: 199601
ENTRY DATE: Entered STN: 19960217
Last Updated on STN: 20000303
Entered Medline: 19960117

AB Oral polymorphonuclear leukocytes (PMN) were obtained from 10 adult donors in good oral health using a method employing repeated mouth rinse collection. Interleukin-1 beta (IL-1 beta) mRNA was detected in freshly obtained cells by blot hybridization of total cellular RNA with a biotin labeled cDNA probe. Supernates from oral PMN placed in culture for 3 hours contained substantial amounts of IL-1 beta measured by ELISA. Significantly greater numbers of PMN and amounts of PMN-derived IL-1 beta were obtained from the same donors 2 hours subsequent to an oral sucrose challenge (3.23 x 10(6) vs. 1.57 x 10(6) mean PMN number, P = 0.004; 59.80 vs. 20.05 mean pg/ml IL-1 beta, P = 0.036, respectively). However, the elevated levels of IL-1 beta were due to the higher cell number rather than to increased production by individual cells. Stimulation of oral PMN with recombinant **granulocyte**-macrophage colony stimulating

NSWER 8 OF 8 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN

ACCESSION NUMBER: 1992:1248 BIOSIS

DOCUMENT NUMBER: PREV199293001248; BA93:1248

TITLE: EFFECTS OF POLYCHLORINATED BIPHENYLS PCB ON CELLULAR FUNCTIONS IN-VITRO.

AUTHOR(S): RAULF M [Reprint author]; KOENIG W

CORPORATE SOURCE: BERUFSGENOSSENSCHAFTLICHES FORSCHUNGSINSTITUT ARBEITSMEDIZIN, INST RUHR-UNIV BOCHUM, GILSINGSTRASSE 14, W-4630 BOCHUM 1

SOURCE: Allergologie, (1991) Vol. 14, No. 9, pp. 352-359.
CODEN: ALLRDI. ISSN: 0344-5062.

DOCUMENT TYPE: Article

FILE SEGMENT: BA

LANGUAGE: GERMAN

ENTRY DATE: Entered STN: 10 Dec 1991
Last Updated on STN: 6 Mar 1992

AB The effects of various isomers of polychlorinated biphenyls (PCBs) to induce and **modulate** the generation of lipoxygenase products from different human cells under noncytotoxic conditions were studied. Various PCB-congeners were potent inducers of platelet aggregation, serotonin-release and 12-HETE-generation. Furthermore, when platelets were incubated with the PCBs the enzymatic steps controlling the metabolism of platelet activating factor (PAF) were modulated. Stimulation of human PMNs with the PCBs did not induce generation of leukotrienes by themselves, but modulated the subsequent opsonized zymosan or sodium fluoride (NaF) induced leukotriene generation. With regard to lymphocyte function (e.g. proliferation, **expression** of CD23 and CD25) the 3,3',4,4',-TCB isomere showed **differential** effects. Our data show a direct relationship between the extent of cell stimulation and chlorosubstitution-pattern of the PCBs.

ANSWER 1 OF 8 MEDLINE on STN
ACCESSION NUMBER: 97028203 MEDLINE
DOCUMENT NUMBER: PubMed ID: 8874218
TITLE: **Differential** effects of interleukin-15 (IL-15) and IL-2 on human neutrophils: modulation of phagocytosis, cytoskeleton rearrangement, gene **expression**, and apoptosis by IL-15.
AUTHOR: Girard D; Paquet M E; Paquin R; Beaulieu A D
CORPORATE SOURCE: Arthritis and Inflammation Research Laboratory, Centre de Recherche du Centre Hospitalier de L'Universite Laval, Ste-Foy, Quebec, Canada.
SOURCE: Blood, (1996 Oct 15) 88 (8) 3176-84.
Journal code: 7603509. ISSN: 0006-4971.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199612
ENTRY DATE: Entered STN: 19970128
Last Updated on STN: 19970128
Entered Medline: 19961202

AB Human neutrophils have been shown recently to express both the beta and the gamma chains of the interleukin-2 receptor (IL-2R). IL-15, a cytokine that has recently been cloned and characterized, was found to share many of the biological functions of IL-2 and is known to mediate signals through IL-2R beta and IL-2R gamma. In recent studies, we observed that IL-2 exerts few effects on various **neutrophil** functions, but information on IL-15-**neutrophil** interactions is lacking. In this study, we observed that IL-15, in contrast to IL-2, induces important morphological cell shape changes that are typical of activated neutrophils. Furthermore, phagocytosis of opsonized sheep red blood cells was significantly increased by IL-15 but not by IL-2. However, similar to IL-2, IL-15 did not **modulate** the oxidative burst response. Furthermore, we observed that de novo RNA synthesis is increased in neutrophils by IL-15 along with de novo protein synthesis, whereas no significant effect of IL-2 was noted. Among the different proteins that were found to be upregulated by IL-15, one was identified by microsequencing as the cytoskeletal protein actin. Finally, we found that IL-15 delays apoptosis of neutrophils more efficiently than IL-2 when evaluated by both microscopic observations and flow cytometry procedures. Furthermore, this phenomenon was dose-dependent (10 to 500 ng/mL), and, at 500 ng/mL, IL-15 delayed apoptosis as strongly as **granulocyte** -macrophage colony-stimulating factor. This study is the first to show that IL-15 is a significant **neutrophil** agonist. Moreover, in view of the differential effects of IL-15 and IL-2 on this cell type, our results support the existence of a specific IL-15R component(s) on human neutrophils.

L10 ANSWER 2 OF 8 MEDLINE on STN
ACCESSION NUMBER: 96231255 MEDLINE
DOCUMENT NUMBER: PubMed ID: 8648912
TITLE: **Differential expression** of macrophage inflammatory protein-2 and monocyte chemoattractant protein-1 in experimental glomerulonephritis.
AUTHOR: Tam F W; Karkar A M; Smith J; Yoshimura T; Steinkasserer A; Kurrle R; Langner K; Rees A J
CORPORATE SOURCE: Department of Medicine, Royal Postgraduate Medical School, Hammersmith Hospital, London, England, United Kingdom.
SOURCE: Kidney international, (1996 Mar) 49 (3) 715-21.
Journal code: 0323470. ISSN: 0085-2538.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English

FILE SEGMENT: Priority Journals
ENTRY MONTH: 199607
ENTRY DATE: Entered STN: 19960805
Last Updated on STN: 19960805
Entered Medline: 19960725

AB We examined the relation between glomerular expression of chemokines from alpha-subfamily (macrophage inflammatory protein-2, MIP-2) and beta-subfamily (monocyte chemoattractant protein-1, MCP-1) and infiltration of neutrophils and monocytes in antibody mediated glomerulonephritis in rats. In the accelerated model of nephrotoxic nephritis (NTN), glomerular expression of MIP-2 and MCP-1 genes correlated with the sequential migration of **neutrophil** and monocyte influx, respectively. These relationships were investigated further in the heterologous phase of NTN by applying various treatments known to **modulate** the severity of injury. Pretreatment with bacterial lipopolysaccharide resulted in greater injury, MIP-2 expression increased 25- to 50-fold, and the glomerular **neutrophil** count increased two- to fourfold. Both MIP-2 mRNA levels and **neutrophil** infiltration were reduced by additional pretreatment with IL-6, IL-1 receptor antagonist, soluble IL-1 receptor or soluble TNF receptor (Spearman correlation coefficient $r = 0.897$, $P < 0.005$). In the heterologous phase of NTN, different pre-treatments only resulted in trivial changes in MCP-1 expression and monocyte infiltration. In conclusion, glomerular MIP-2 gene expression correlates with **neutrophil** infiltration both temporally during the evolution of nephritis, and when glomerular injury is modified by treatment. Glomerular MCP-1 gene expression correlates with monocyte influx. The data show chemokines of alpha- and beta-subfamilies co-operative to cause selective and sequential migration of different leukocyte subsets during development of antibody mediated glomerulonephritis.

L10 ANSWER 3 OF 8 MEDLINE on STN
ACCESSION NUMBER: 94014398 MEDLINE
DOCUMENT NUMBER: PubMed ID: 8409417
TITLE: TGF-beta is a bidirectional modulator of cytokine receptor **expression** on murine bone marrow cells. **Differential** effects of TGF-beta 1 and TGF-beta 3.
AUTHOR: Jacobsen S E; Ruscetti F W; Roberts A B; Keller J R
CORPORATE SOURCE: Laboratory of Leukocyte Biology, National Cancer Institute, Bethesda, MD 20892.
CONTRACT NUMBER: NO1-CO-74102 (NCI)
SOURCE: Journal of immunology (Baltimore, Md. : 1950), (1993 Nov 1) 151 (9) 4534-44.
Journal code: 2985117R. ISSN: 0022-1767.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199311
ENTRY DATE: Entered STN: 19940117
Last Updated on STN: 19940117
Entered Medline: 19931117

AB Transforming growth factor beta (TGF-beta), an immunomodulator, has inhibitory as well as stimulatory effects on bone marrow cells. In this study, we demonstrate that TGF-beta 1 also is a bidirectional modulator of CSF receptor expression on murine bone marrow cells. TGF-beta 1 up-regulated **granulocyte**-macrophage (GM)-CSF receptor expression in a time- and dose-dependent manner, with a maximum up-regulation of 64% by 48 h at 20 ng/ml. In contrast, TGF-beta 1 down-modulated IL-3 and CSF-1 receptor expression by 54 and 55%, respectively, by 24 h. TGF-beta 1 did not affect G-CSF receptor expression, in agreement with its inability to affect G-CSF-induced proliferation. The CSF receptor modulation induced by TGF-beta 1 preceded its effects on CSF-stimulated

proliferation. The effects of TGF-beta on CSF receptor expression were isoform dependent, thus TGF-beta 3 was a 10-fold more potent inhibitor of both IL-3-induced colony formation and IL-3 receptor expression than TGF-beta 1, whereas TGF-beta 1 was a more potent stimulator of GM-CSF-stimulated colonies and GM-CSF receptor expression than TGF-beta 3. Therefore, the ability of TGF-beta to **modulate** the CSF receptor density/cell and/or the actual number of progenitors expressing CSF receptors directly correlates with the multifunctional effects of TGF-beta in hematopoiesis.

L10 ANSWER 4 OF 8 EMBASE
on STN

ACCESSION NUMBER: 97376059 EMBASE
DOCUMENT NUMBER: 1997376059
TITLE: Modulation of AUUUA response element binding by heterogeneous nuclear ribonucleoprotein A1 in human T lymphocytes: The roles of cytoplasmic location, transcription, and phosphorylation.
AUTHOR: Hamilton B.J.; Burns C.M.; Nichols R.C.; Rigby W.F.C.
CORPORATE SOURCE: W.F.C. Rigby, Sec. of Connective Tissue Diseases, Dept. of Medicine, Dartmouth-Hitchcock Medical Center, Lebanon, NH 03756, United States. rigby@dartmouth.edu
SOURCE: Journal of Biological Chemistry, (1997) 272/45 (28732-28741).
Refs: 68
ISSN: 0021-9258 CODEN: JBCHA3
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 026 Immunology, Serology and Transplantation
029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English

AB The heterogeneous nuclear ribonucleoprotein A1 (hnRNP A1) shuttles between the cytoplasm and nucleus and plays important roles in RNA metabolism. Whereas nuclear hnRNP A1 has been shown to bind intronic sequences and **modulate** splicing, cytoplasmic hnRNP A1 is associated with poly(A)+ RNA, indicating different RNA ligand specificity. Previous studies indicated that cytoplasmic hnRNP A1 is capable of high-affinity binding of reiterated AUUUA sequences (ARE) that have been shown to **modulate** mRNA turnover and translation. Through a combination of two-dimensional gel and proteolysis studies, we establish hnRNP A1 (or structurally related proteins that are post-translationally regulated in an identical manner) as the dominant cytoplasmic protein in human T lymphocytes capable of interacting with the ARE contained within the context of full-length **granulocyte**- macrophage colony-stimulating factor mRNA. We additionally demonstrate that cytoplasmic hnRNP A1 preferentially binds ARE relative to pre-mRNAs in both cross-linking and mobility shift experiments. RNA polymerase II inhibition increased the binding of ARE (AUBP activity) and poly(U)-Sepharose by cytoplasmic bnRNP A1, while nuclear hnRNP A1 binding was unaffected. Nuclear and cytoplasmic hnRNP A1 could be distinguished by the **differential** sensitivity of their RNA binding to diamide and N-ethylmaleimide. The increase in AUBP activity of cytoplasmic hnRNP A1 following RNA polymerase II inhibition correlated with serine-threonine dephosphorylation, as determined by inhibitor and metabolic labeling studies. Thus, cytoplasmic and nuclear hnRNP A1 exhibit different RNA binding profiles, perhaps transduced through serine-threonine phosphorylation. These findings are relevant to the specific ability of hnRNP A1 to serve distinct roles in post-transcriptional regulation of gene **expression** in both the nucleus and cytoplasm.

L10 ANSWER 5 OF 8 EMBASE
on STN

ACCESSION NUMBER: 96055000 EMBASE
DOCUMENT NUMBER: 1996055000
TITLE: Reactivity of purified complement component 3b with bovine neutrophils and modulation of complement receptor 1.
AUTHOR: Di Carlo A.L.; Paape M.J.; Miller R.H.
CORPORATE SOURCE: USDA-ARS, Milk Secretion/Mastitis Laboratory,Beltsville, MD 20705, United States
SOURCE: American Journal of Veterinary Research, (1996) 57/2 (151-156).
ISSN: 0002-9645 CODEN: AJVRAH
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 025 Hematology
029 Clinical Biochemistry
030 Pharmacology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English

AB Objective. To study binding of purified complement component C3b to bovine blood and mammary neutrophils (PMN) after various treatments and determine their ability to **modulate** receptor numbers. Design. Cell isolation, activation, and flow cytometric studies. Animals. Healthy lactating Holstein cattle. Procedure. Complement component C3b (18,300 kd) was isolated from bovine serum by column chromatography, and flow cytometric assays using fluorescein isothiocyanate-labeled C3b were developed to evaluate binding to PMN complement receptor 1. Multiple substances were tested to determine their overall effect on C3b binding to PMN. Blood and milk PMN were isolated by **differential** centrifugation and exposed to optimal concentrations of recombinant human C5a, formyl-methyl leucyl phenylalanine, recombinant bovine interferon-γ, variable concentrations of phorbol myristate acetate (0.01 to 100 ng), calcium ionophore A23187, serum-opsonized zymosan, zymosan-activated serum (ZAS), zymosan-activated plasma (ZAP), and hydrocortisone acetate (25 and 70 ng). Additionally, mammary and blood PMN were preincubated in skim milk and whey. Results. Variable concentrations of phorbol myristate acetate caused a dose-dependent increase in percentage of PMN binding C3b, and increased the amount of C3b bound per cell. Significant increases were observed after PMN treatment with calcium ionophore, serum opsonized zymosan, ZAS, and ZAF; conversely, incubation of PMN with hydrocortisone acetate resulted in reduced overall binding of C3b. Mammary PMN consistently bound more C3b, which was attributed to their activation during migration into the mammary gland. Binding of C3b was inhibited by skim milk. Activation of blood PMN with PMA, ZAS, and ZAF elicited larger responses than those observed for mammary PMN. Conclusions. Modulation of complement receptors on bovine PMN is possible. Additionally, significant difference between the level of binding of C3b to blood and milk PMN, with milk PMN having higher binding, may be attributable to migration of PMN into the mammary gland, causing increased receptor **expression**. Clinical Relevance. Contribution to a greater understanding of the role of complement in bovine immunologic systems, leading to testing for in vivo enhancement of bovine immune responses to invading pathogens.

L10 ANSWER 6 OF 8 on STN
ACCESSION NUMBER: 91234937 EMBASE
DOCUMENT NUMBER: 1991234937
TITLE: Production of **granulocyte**/macrophage-colony-stimulating factor by human natural killer cells: Modulation by the p75 subunit of the interleukin 2 receptor and by the CD2 receptor.
AUTHOR: Levitt L.J.; Nagler A.; Lee F.; Abrams J.; Shatsky M.; Thompson D.

CORPORATE SOURCE: Hematology Division, Stanford University, Medical Center,Stanford, CA 94305, United States
SOURCE: Journal of Clinical Investigation, (1991) 88/1 (67-75). ISSN: 0021-9738 CODEN: JCINAO
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 026 Immunology, Serology and Transplantation
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English

AB Resting natural killer (NK) cells express the p75 chain of the IL-2 receptor (IL-2Rβ) and most NK cells express the CD2 (erythrocyte rosette) receptor. The cell adhesion molecule, LFA-3, is a natural co-ligand for CD2. Tac antigen (IL-2Rα), a p55 IL-2R subunit, can be expressed after NK activation and may play a role in IL-2-induced NK proliferation. Little is known of the molecular mechanisms underlying cytokine production in NK cells. We investigated the roles of IL-2Rα, IL-2Rβ, and CD2/LFA-3 in the molecular regulation of NK cell **granulocyte**/macrophage-colony-stimulating factor (GM-CSF) production. Enriched populations of peripheral blood NK cells were separated into CD16-positive and CD16-negative fractions by flow cytometry; positively selected cells were > 97% positive for CD16 (the FcIII receptor for IgG which is present on almost all NK cells), < 1% positive for the T cell antigen CD3, and did not demonstrate rearrangement of the T cell receptor β chain gene by Southern blot. NK cell supernatants were harvested after 3-4 d of incubation with 0-100 U/ml IL-2, or after incubation with anti-CD2 (T113) MAb and sheep red blood cells (SRBC are a homologue for LFA-3). Parallel cell aliquots were harvested at 3-16 h for transcriptional run-on assays, S1 nuclease assays, and actinomycin D mRNA t(1/2) determinations. IL-2-activated NK supernatants contained large amounts of GM-CSF (178±35 pg/ml) by ELISA as did supernatants from CD2-activated NK cells (T113 MAb + SRBC: 212±42) vs. < 20 pg/ml for NK cells incubated alone or with either SRBC or T113 MAb alone. Sepharose-linked anti-CD3 MAb did not induce GM-CSF release from NK cells. By S1 analysis, both IL-2 and CD2 stimulation markedly augmented GM-CSF mRNA **expression** but with very different latencies of onset. IL-2Rβ MAb inhibited > 85% of GM-CSF release from IL-2-activated NK cells and markedly suppressed IL-2-induced GM-CSF mRNA **expression**, whereas IL-2Rα MAb even at 2,000-fold molar excess of IL-2 had little effect (< 10%) on either GM-CSF release or mRNA **expression**. Run-on assays showed that GM-CSF is constitutively transcribed in NK cells and that IL-2 and CD2-activated cells had a three- to fourfold increased rate of GM-CSF transcription compared to nonstimulated cells. The t(1/2) of GM-CSF mRNA in IL-2-activated NK cells was identical to that of unstimulated NK cells (15 min), whereas GM-CSF mRNA t(1/2) in CD2-activated NK cells was increased 2.5-fold. We conclude that GM-CSF production in NK cells is regulated by both the IL-2Rβ and the CD2 receptor but not by IL-2Rα, that both transcriptional and posttranscriptional signals act together to **modulate** the level of GM-CSF mRNA in NK cells, and that the molecular mechanisms underlying NK cell GM-CSF production are dependent in part on **differential** surface receptor activation.

L10 ANSWER 7 OF 8 EMBASE on STN
ACCESSION NUMBER: 91102370 EMBASE
DOCUMENT NUMBER: 1991102370
TITLE: Modulation of monocyte chemotactic function in inflammatory lesions. Role of inflammatory mediators.
AUTHOR: Katona I.M.; Ohura K.; Allen J.B.; Wahl L.M.; Chenoweth D.E.; Wahl S.M.
CORPORATE SOURCE: Department of Pediatrics, Uniformed Services Univ.,Bethesda, MD 20814-4799, United States

SOURCE: Journal of Immunology, (1991) 146/2 (708-714).
ISSN: 0022-1767 CODEN: JOIMA3
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 005 General Pathology and Pathological Anatomy
025 Hematology
026 Immunology, Serology and Transplantation
031 Arthritis and Rheumatism
LANGUAGE: English
SUMMARY LANGUAGE: English

AB Monocyte recruitment and accumulation in the synovial tissue is pivotal in the evolution of rheumatoid arthritis (RA). In the present study we examined the chemotactic potential of monocytes obtained from synovial fluid (SF) of patients with RA. Functionally, SF monocytes exhibited greatly diminished chemotactic activity to C5a compared with monocytes from the peripheral blood. In contrast, their chemotactic responsiveness to the synthetic peptide, FMLP, was nearly normal. To define a mechanism for this **differential** chemotactic dysfunction, cell-surface receptors for C5a (C5aR) and FMLP (FMLP-R) were evaluated. Whereas FMLP-R **expression** was similar on both blood and inflammatory monocytes, C5aR **expression** was markedly reduced on SF cells. Because decreased C5a binding in certain RA SF samples could not be attributed to free C5a, known or suspected components of inflammatory SF were evaluated for their ability to **modulate** chemotactic ligand receptors. Bacterial products including LPS and streptococcal cell walls, which are potent monocyte activators, down-regulated C5aR without affecting FMLP-R. Moreover, the cytokines IFN-γ and **granulocyte** -macrophage-CSF selectively decreased C5aR in parallel with decreased in vitro chemotactic activity to C5a. Thus, these data indicate that 1) synovial effusions may contain C5a and/or inflammatory mediators that **modulate** phenotypic and functional changes in monocytes, 2) chemotactic ligand receptors are independently regulated in inflammatory lesions, and 3) decreased C5aR **expression** and chemotactic potential likely provide a mechanism whereby monocyte-macrophages persist within the inflamed synovium.

L10 ANSWER 8 OF 8 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 1992:1248 BIOSIS
DOCUMENT NUMBER: PREV199293001248; BA93:1248
TITLE: EFFECTS OF POLYCHLORINATED BIPHENYLS PCB ON CELLULAR FUNCTIONS IN-VITRO.
AUTHOR(S): RAULF M [Reprint author]; KOENIG W
CORPORATE SOURCE: BERUFSGENOSSENSCHAFTLICHES FORSCHUNGSINSTITUT ARBEITSMEDIZIN, INST RUHR-UNIV BOCHUM, GILSINGSTRASSE 14, W-4630 BOCHUM 1
SOURCE: Allergologie, (1991) Vol. 14, No. 9, pp. 352-359.
CODEN: ALLRDI. ISSN: 0344-5062.
DOCUMENT TYPE: Article
FILE SEGMENT: BA
LANGUAGE: GERMAN
ENTRY DATE: Entered STN: 10 Dec 1991
Last Updated on STN: 6 Mar 1992

AB The effects of various isomers of polychlorinated biphenyls (PCBs) to induce and **modulate** the generation of lipoxygenase products from different human cells under noncytotoxic conditions were studied. Various PCB-congeners were potent inducers of platelet aggregation, serotonin-release and 12-HETE-generation. Furthermore, when platelets were incubated with the PCBs the enzymatic steps controlling the metabolism of platelet activating factor (PAF) were modulated. Stimulation of human PMNs with the PCBs did not induce generation of leukotrienes by themselves, but modulated the subsequent opsonized zymosan or sodium fluoride (NaF) induced leukotriene generation. With regard to lymphocyte function (e.g. proliferation, **expression** of CD23 and

CD25) the 3,3',4,4',-TCB isomere showed **differential** effects.
Our data show a direct relationship between the extent of cell stimulation and chlorosubstitution-pattern of the PCBs.